Long-term Consequences of the Early Treatment of Children with Congenital Hypothyroidism Detected by Neonatal Screening in Nanjing, China: a 12-year Follow-up Study

Summary
This study was performed to investigate the prevalence of congenital hypothyroidism (CH) in neonates in Nanjing, China and the long-term consequences of early treatment. A total of 442,454 neonates were screened for CH and 183 neonates were confirmed, with a prevalence of 1 in 2418. Of these, 163 neonates completed the follow-up process and 163 healthy children were recruited as the control group. The height, weight and body mass index (BMI) of the children with CH from 0.5 to 6 years were not significantly different from the control group (p > 0.05). The children with CH had a significantly increased risk for being overweight or obese between 0.5 and 6 years (p < 0.05). The children with CH showed a significantly lower developmental quotient (DQ) than the control group in all four areas of the Gesell test (p < 0.05). The results suggest that children with CH that has been identified by newborn screening and early treatment have normal growth and neuromotor development.

Key words: congenital hypothyroidism, neonatal screening, growth, developmental delay, obesity.

Introduction
Congenital hypothyroidism (CH) is one of the most common causes of brain damage and mental retardation; it occurs in approximately 1 in 2000 to 1 in 4000 newborns [1–3]. There was an inverse relationship between age at diagnosis and intelligence quotient (IQ) later in life; the longer the condition is undetected, the lower the IQ [4]. We performed a population-based study to demonstrate the prevalence of CH in Nanjing, China and to evaluate the long-term consequences in children with CH detected by neonatal screening and treated early over a 12-year follow-up period.

Materials and Methods
This prospective cohort study was performed in a regional screening center, Nanjing, China, between 1 January 1998 and 31 December 2009. Blood samples were taken and thyroid stimulating hormone (TSH) levels were measured by dissociation-enhanced lanthanide fluoroimmunoassay (Perkin Elmer, Turku, Finland). Infants who were confirmed to have CH were instantly treated with thyroxine replacement therapy. Length and height was measured at the ages of 0.5, 1, 2, 3, 4, 5 and 6 years. Body mass index (BMI) was calculated by dividing body weight (kg) by the square of the height (m²). A developmental assessment was conducted at 24 months using the Gesell Developmental Schedules. Data were analyzed with SPSS® 16.0. The odds ratio (OR) and its 95% confidence interval (CI) were computed for dichotomous outcomes. The study was approved by the ethics committee of the Nanjing Maternal and Child Health Hospital. The parents gave written informed consent.

Results
A total of 442,0454 neonates were screened for CH and 183 neonates were confirmed, with a prevalence of 1 in 2418. Of these, 163 neonates completed the follow-up process and 163 healthy children were recruited as the control group. The height, weight and BMI of the children with CH from 0.5 to 6 years were not significantly different from the control group (p > 0.05). But, the result showed that children with CH had an increased prevalence of overweight and obese (Table 1).

The children with CH showed significantly lower developmental quotient (DQ) levels than the control group in all four areas of the Gesell test (p < 0.05). Most infants (73.5%) showed normal schedules and 26 children (26.5%) exhibited developmental delay in one or more features of the Gesell Schedules, as follows: 2.0% showed motor impairment; 4.1% presented with developmental delay in the personal social behavior; 6.1% had language deficits; and 14.3% had multiple impairments (3.1% motor and language; 4.1% motor, language and adaptive; and 7.1% motor, language, adaptive and personal social behavior).

Table 1
The OR of being overweight or obese with congenital hypothyroidism aged between 6 months and 6 years

<table>
<thead>
<tr>
<th>Follow-up time</th>
<th>6 months</th>
<th>12 months</th>
<th>2 years</th>
<th>3 years</th>
<th>4 years</th>
<th>5 years</th>
<th>6 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boys OR (95% CI)</td>
<td>3.24 (1.51–6.97)</td>
<td>3.30 (1.54–7.07)</td>
<td>4.41 (1.81–10.77)</td>
<td>3.06 (1.23–7.64)</td>
<td>3.83 (1.39–10.55)</td>
<td>3.67 (1.14–11.79)</td>
<td>4.64 (1.06–20.38)</td>
</tr>
<tr>
<td>Girls OR (95% CI)</td>
<td>3.16 (1.48–6.76)</td>
<td>4.55 (2.18–9.51)</td>
<td>3.57 (1.66–7.67)</td>
<td>3.20 (1.40–7.30)</td>
<td>3.73 (1.43–9.75)</td>
<td>3.43 (1.03–11.48)</td>
<td>4.38 (1.03–18.63)</td>
</tr>
</tbody>
</table>
Discussion

Our data showed a prevalence of CH in a regional screening center of China of 1 in 2418 newborns over the previous 12-year period. This is comparable to the prevalence levels reported for neighboring Japan (1 in 2864) [5]. In general, children with CH detected by neonatal screening who received early treatment had normal growth. But our results suggested that there was a marked increase in the prevalence of CH infants who were overweight or obese, which was consistent with reports that the BMI values of children with CH were steadily higher than the 95th centile during the first 6 years of life [6]. It is thought that children with CH generally weigh more than their peers and show a loss of BMI plasticity during the first years of life, possibly as an extended result of fetal and neonatal hypothyroidism [7]. The factor that caused this phenomenon is still poorly understood and requires further investigation. The observations in our study indicated that the detection of CH, early treatment and follow-up in our country is likely to have a beneficial effect on reducing the impact of this disease.

QING SUN,* YU-LIN CHEN,* ZHANG-BIN YU, SHU-PING HAN, XIAO-YUE DONG, YU-FANG QIU, LI SHA, and XI-RONG GUO

Department of Pediatrics, Nanjing Maternal and Child Health Hospital Affiliated to Nanjing Medical University, Nanjing 210004, China
doi:10.1093/tropej/fmr010
Advance Access published on 4 February 2011

References


Acknowledgements

We thank Dr Tao Jiang (Neonatal Screening center of the Nanjing Maternal and Child Health Hospital of Nanjing Medical University) for providing some data.

Correspondence: Shu-Ping Han and Zhang-Bin Yu, Department of Pediatrics, Nanjing Maternal and Child Health Hospital, Nanjing Medical University, No. 123 Tian Fei Xiang, Mo Chou Road, Nanjing 210004, China. E-mail: <shupinghan@njmu.edu.cn; zhangbinyu@njmu.edu.cn>.

*These authors contributed equally to this work.

Experience of Setting up a Microbiology Service for Rural Facility-Based Sick Newborn Care Unit

Studies across the developing world have shown that infection is a major cause of neonatal and childhood morbidity and mortality in rural setting [1, 2]. Documentation of the burden of infection in this population, including microbial aetiology is, however, scanty. Due to lack of resources, blood culture is an irregularly used investigation, largely restricted to urban and semi-urban tertiary centres in India [3]. Microbiology laboratory support is usually not available in rural health-care facilities in resource-poor settings. Treatment of infection, by default, remains empirical. In order to achieve a uniform level of care across urban and rural neonatal units, alternative approaches for laboratory facilities need to be considered. The present study describes a system to provide microbiological facility to a remote rural facility-based sick newborn unit in India. This unit at Suri Sadar Hospital, Birbhum, was the second unit to be developed in India, based on the Purulia model [4].

Laboratory support was provided from a nodal centre at Kolkata, located 220 km from the rural unit. The preparatory phase included interactive visits to the study site, onsite training, development of guidelines and standard operating procedures. Variations in data observed due to individual difference in use of terminology were standardized. Patient information was collected and blood for culture was drawn for babies with clinical sepsis or perinatal risk factors. Specimen transport was done thrice a week. Blood culture was performed by BACTEC 9050. Delayed entry of vials proved to be an acceptable methodology. Identification was performed by conventional methods and confirmed by using ID32E, ID32GN and ID32C kits (bioMérieux, Marcyl’Etoile, France). Kirby Bauer disc diffusion